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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/077,698 | 02/13/2002 | Maria Alexandra Glucksmann | MNI-204CP2DV1 | 4059 |

30405 7590 07/25/2005

MILLENNIUM PHARMACEUTICALS, INC.
40 Landsdowne Street
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| EXAMINER | |
|---|---|
| BRANNOCK, MICHAEL T | |
| **ART UNIT** | **PAPER NUMBER** |
| 1649 | |

DATE MAILED: 07/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/077,698 | GLUCKSMANN ET AL. | |
| | Examiner | Art Unit | |
| | Michael Brannock | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *24-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *24-33* is/are allowed.

6)☐ Claim(s) *34-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

***Status of Application: Claims and Amendments***

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Applicant is notified that the amendments put forth on 5/9/05, have been entered in full.

***Response to Amendment***

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

***Information Disclosure Statement***

The information disclosure statement filed July 9, 2002 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP ∋ 609 because citations A9 and A12 lack sufficient description so as to lead the reader to the cited documents.

Applicant argues that a complete descriptions are provided in supplemental information disclosure statement filed May 9, 2005. This argument has been fully considered but not deemed persuasive.

The May 9, 2005IDS also fails to comply for the essentially the same reason. As set forth previously regarding the objection to the specification, the attempt to incorporate subject matter into this application by reference to active Internet sites (i.e., hyperlinks) is improper because such web sites are constantly being changed and updated. A change or update of the web site would automatically raise the issue of new matter, because the updated information was

not known to the inventors at the time of the filing of the instant specification. Also, the organization, views and accuracy of the information contained on commercial web sites is not under the control of the PTO. Thus, one could not be sure that the material on the website at any time in the future was the same material that applicant requests the examiner to consider. Thus, this website has not been considered by the examiner. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP ∋ 609 & C(1).

**Maintained Rejections:**

Claims 34-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling polynucleotides encoding a polypeptide of SEQ ID NO: 1 and 4 and for naturally occurring polynucleotides that hybridize under the conditions recited at page 44 lines 19 and 20 to the polynucleotides of SEQ ID NO: 2 and 5 wherein elevated levels of said naturally occurring polynucleotides are indicative of cardiac myocyte hypertrophy, does not reasonably provide enablement for polynucleotides comprising complements of said polynucleotides, that do not hybridize as described above, as set forth previously.

Applicant argues that if polynucleotides that hybridize are enabled, then polynucleotides that are 95% identical should be enabled as well because the latter is more definite. This argument has been fully considered but not deemed persuasive. The basis of the rejection is not

one of definitude. Simply verbalizing a percent identity describes no particular sequence nor does it provide enablement for such.

Applicant argues that structural features of the encoded protein are taught as well as conservative substitutions. This argument has been fully considered but not deemed persuasive. The specification has not taught what particular substitutions can be made. As set forth previously, certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Applicant argues that functional assays are taught. This argument has been fully considered but not deemed persuasive. No functional assays have been taught. There is no teaching of an assay that would identify functional variants and nothing regarding comparing the nucleic acid levels of 14273 variants in normal versus hypertrophic cardiac myocytes is present in the specification. There is no teaching that changes in level of 14273 expression identify variants of 14273.

Applicant argues that antibodies to variants are not required by the claims. This argument has been fully considered but not deemed persuasive. The examiner was simply

detailing the scope of enablement provided by the specification and the well known use of polynucleotides to generate polypeptides for use in antibody production.

Claims 34-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a human and murine polynucleotide of SEQ ID NO: 2 and 5, respectively, yet the claims encompass polynucleotides not described in the specification, i.e. polynucleotides sequences from other species, mutated sequences, allelic variants, or sequences need that need only be 95% identical to SEQ ID NO: 2 or 5, as set fourth previously.

Applicant argues that polynucleotides 95% identical to SEQ ID NO: 2 or 5 could be readily envisioned and that it would be routine to test each to determine if such a variant would also have the characteristic of elevated nucleic acid levels being indicative of cardiac hypertrophy. This argument has been fully considered but not deemed persuasive. The examiner can find no specific teaching in the specification as to how this could be done and thus one skilled in the art would not consider that Applicant was in possession of such a tremendous genus.

Applicant argues that Example 14 of the Written Description Guidelines provides that recitation of percent identify in combination with a functional limitation to a genus is an accepted method of describing and claiming a genus. This argument has been fully considered but not deemed persuasive. First, Example 14 is directed to polypeptides whereas the instant

claims are directed to nucleic acid molecules. Applicant is reminded that Example 14 includes an important fact in the pattern that is not present here. Example 14 stipulates that "procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity", and that in addition to this requirement (moreover) "procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art." There does not appear to be any conventional art-recognized procedures that produce polynucleotide variants of SEQ ID NO: 2 or 5 that are 95% identical to SEQ ID NO: 2 or 5 and yet retain any useful activity. Additionally, one skill in the art appreciates that simply verbalizing that a polynucleotide should have some function does not put one in possession of such a polynucleotide.

***Allowable Subject Matter***

Claims 24-33 are allowed.

## *Conclusion*

Please note the new central fax number for official correspondence below:

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX months.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

July 19, 2005

ELIZABETH KEMMERER
PRIMARY EXAMINER